<u>AMENDMENTS TO THE CLAIMS</u>

Claims 1-23 (canceled).

Claim 24 (currently amended): A method of detecting a disease or a disease susceptibility trait in an organism, wherein said disease or said disease susceptibility trait ~~is known to be~~ <u>has been</u> associated with a germline mutation that causes an about 50% decrease in the level of wild-type protein <u>expressed by one of two or more subject genes in affected individuals relative to the level of said wild-type protein</u> normally expressed by <u>the same</u> ~~any of two or more~~ subject ~~genes~~ <u>gene in unaffected individuals</u>, wherein said germline mutation is selected from the group consisting of truncation-causing mutations, mutations that cause allelic loss, and mutations that cause the expression of proteins with non-wild-type epitopes, and wherein each of said subject genes ~~is known to be~~ <u>has been</u> associated with such a disease or such a disease susceptibility trait, comprising:

(a) isolating a biological sample containing normal cells from said organism;

(b) preparing a lysate of said normal cells;

(c) preparing a protein extract from said lysate of said normal cells;

(d) immunologically quantitating the amount of wild-type protein expressed by each of the subject genes in said protein extract of said normal cells;

(e) calculating the ratio of the amount of the wild-type protein expressed by one of said subject genes in said normal cells, to the amount of wild-type protein expressed by the other subject gene in said normal cells, or to each of the amounts of wild-type protein expressed by each of the other subject genes in said normal cells; and

(f) determining whether the ratio or ratios calculated in step (e) reflects or reflect an about 50% decrease in the normal level of a wild-type protein expressed by either of the subject genes, or by any of the subject genes in said normal cells;

(g) whereby if the ratio or ratios calculated in step (e) indicates or indicate that there is an about 50% decrease in the normal level of a wild-type protein expressed

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by one of the subject genes in said normal cells, that that subject gene contains a germline mutation in one of its alleles, and that the subject organism is affected by the disease or the disease susceptibility trait associated with said germline mutation.

Claim 25 (previously presented): The method of Claim 24 wherein step (f) comprises comparing the ratio or ratios calculated in step (e) to a comparable mean or means of ratios calculated from the amounts of wild-type proteins expressed by the subject genes in comparable biological samples from organisms of the same taxonomic classification as the subject organism, wherein said organisms of the same taxonomic classification as the subject organism are unaffected by said disease or by said disease susceptibility trait.

Claim 26 (original): The method of Claim 24 wherein said organism is a vertebrate.

Claim 27 (original): The method of Claim 26 wherein said vertebrate is a mammal.

Claim 28 (original): The method of Claim 27 wherein said mammal is a human.

Claims 29-31 (canceled).

Claim 32 (previously presented): The method of Claim 24 wherein said mutation is selected from the group consisting of nonsense mutations, frameshift mutations, promoter mutations, enhancer mutations, splice site mutations, null mutations, and poly-A tail mutations.

Claim 33 (previously presented): The method of Claim 24 wherein said biological sample is selected from the group consisting of body fluids and tissue specimens.

Claim 34 (original): The method of Claim 33 wherein said body fluids are selected from the group consisting of blood, serum, plasma, semen, breast exudate, gastric secretions, fecal suspensions, bile, saliva, tears, sputum, mucous, urine, lymph, cytosols, ascites, pleural effusions, amniotic fluid, bladder washes, bronchoalveolar lavages, and cerebrospinal fluid.

Claim 35 (previously presented): The method of Claim 24 wherein said normal cells are peripheral blood lymphocytes.

Claim 36 (canceled).

Claim 37 (original): The method of Claim 24 wherein said method is diagnostic or diagnostic/prognostic for cancer or for susceptibility to cancer.

Claim 38 (original): The method of Claim 24 wherein the subject genes are selected from the group consisting of ATM, APC, BRCA1, BRCA2, CFTR, c-myb, dystrophin, E-cadherin, EMD, FAA, IDS, MLH1, MSH2, MSH6, NF1, NF2, p16, PKD1, PKD2, PMS1, PMS2, PTCH, TGFBR2, and VHL genes.

Claim 39 (original): The method of Claim 24 wherein said disease is, or said susceptibility trait is for a disease selected from the group consisting of ataxia-telangiectasia, hemangioblastoma, renal cell carcinoma, pheochromocytoma, colon cancer, colorectal cancer, gastrointestinal cancer, breast cancer, ovarian cancer, endometrial cancer, prostate cancer, pancreatic cancer, biliary tract cancer, cystic fibrosis, hematologic malignancies, Duchenne muscular dystrophy, genitourinary cancers, gynecologic cancers, Emery-Dreifuss muscular dystrophy, Fanconi anemia, Hunter syndrome, neurofibromatosis type 1, neurofibromatosis type 2, familial melanoma, polycystic kidney disease, nevoid basal carcinoma, and von Hippel-Lindau disease.

Claim 40 (original): The method of Claim 24 wherein the subject genes are mismatch repair genes.

Claim 41 (original): The method of Claim 40 wherein the subject genes are selected from the group consisting of the MLH1, MSH2, MSH6, PMS1, and PMS2 genes; and said disease is or said disease susceptibility trait is for hereditary non-polyposis colon cancer.

Claim 42 (original): The method of Claim 41 wherein the subject genes are the MLH1 gene and the MSH2 gene.

Claim 43 (previously presented): The method of Claim 24 wherein the amount of each wild-type protein expressed by each subject gene is determined by Western blot analysis, by immunoprecipitation and then by Western blot analysis, by flow cytometry, by EIA, by ELISA, by RIA, by competition immunoassay, by dual antibody sandwich assay, by chemiluminescent assay, by bioluminescent assay, by fluorescent assay, or by agglutination assay.

Claim 44 (original): The method of Claim 24 which is automated.

Claims 45-54 (canceled).

Claim 55 (previously presented): A method according to Claim 25 wherein the ratio or ratios calculated in step (e) when compared to said mean or means of ratios indicates that the about 50% decrease in the normal level of said wild-type protein expressed by one of the subject genes in said sample is about 50% ± 20% of the level of said wild-type protein in comparable samples from organisms unaffected by said disease or said disease susceptibility trait.

Claim 56 (previously presented): A method according to Claim 25 wherein the ratio or ratios calculated in step (e) when compared to said mean or means of ratios

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indicates that the about 50% decrease in the normal level of said wild-type protein expressed by one of the subject genes in said sample is about 50% ± 15% of the level of said wild-type protein in comparable samples from organisms unaffected by said disease or said disease susceptibility trait.

Claim 57 (previously presented): A method according to Claim 25 wherein the ratio or ratios calculated in step (e) when compared to said mean or means of ratios indicates that the about 50% decrease in the normal level of said wild-type protein expressed by one of the subject genes in said sample is about 50% ± 10% of the level of said wild-type protein in comparable samples from organisms unaffected by said disease or said disease susceptibility trait.

Claim 58 (canceled).

Claim 59 (previously presented): The method of Claim 40 wherein the normal biological sample comprises peripheral blood lymphocytes.

Claim 60 (previously presented): The method of Claim 42 wherein the normal biological sample comprises peripheral blood lymphocytes.

Claim 61 (previously presented): The method of Claim 24 wherein said mutation is selected from the group consisting of truncation-causing mutations and mutations that cause allelic loss.

Claim 62 (previously presented): The method of Claim 24 wherein said two or more subject genes are associated with the same disease or the same disease susceptibility trait.

Claim 63 (previously presented): The method of Claim 62 wherein said subject genes are selected from the group consisting of MLH1, MSH2, MSH6, PMS1,

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PMS2, APC and E-cadherin, and said disease is or said disease susceptibility trait is for colon cancer.

Claim 64 (previously presented): The method of Claim 62 wherein said subject genes are selected from the group consisting of BRCA1, BRCA2 and E-cadherin, and said disease is or said disease susceptibility trait is for breast cancer.

Claim 65 (previously presented): The method of Claim 62 wherein said subject genes are NF1 and NF2, and said disease is or said disease susceptibility trait is for neurofibromatosis.

Claim 66 (previously presented): The method of Claim 62 wherein said subject genes are PKD1, PKD2 and VHL, and wherein said disease or said disease susceptibility trait is for kidney disease.

Claim 67 (previously presented): The method of Claim 24 wherein said two or more subject genes are associated with different diseases or different disease susceptibility traits.

Claim 68 (previously presented): The method of Claim 67 wherein step (f) comprises comparing the ratio or ratios calculated in step (e) to a comparable mean or means of ratios calculated from the amounts of wild-type proteins expressed by the subject genes in comparable biological samples from organisms of the same taxonomic classification as the subject organism, wherein said organisms of the same taxonomic classification as the subject organism are unaffected by said diseases or by said disease susceptibility traits.

Claim 69 (previously presented): The method of Claim 67, wherein said subject genes are selected from the group consisting of MLH1, MSH2, MSH6, PMS1, PMS2, APC, BRCA1, BRCA2, and E-cadherin, and wherein said diseases are or said

disease susceptibility traits are for colorectal, breast, endometrial, ovarian, prostate, stomach, small intestine, pancreatic and biliary tract cancers.

Claim 70 (previously presented): The method of Claim 67, wherein said subject genes are selected from the group consisting of mismatch repair genes, BRCA1, BRCA2, and E-cadherin, and wherein said diseases are or said disease susceptibility traits are for hereditary non-polyposis colon cancer and breast cancer.

Claim 71 (previously presented): The method of Claim 67, wherein said subject genes are selected from the group consisting of adenomatous polyposis coli, BRCA1, BRCA2, and E-cadherin, and wherein said diseases are or said disease susceptibility traits are for familial adenomatous polyposis and breast cancer.

Claim 72 (previously presented): The method of Claim 67, wherein said subject genes are selected from the group consisting of the MLH1, MSH2, MSH6, PMS1, PMS2, and APC genes, and wherein said diseases are or said disease susceptibility traits are for hereditary non-polyposis colon cancer and familial adenomatous polyposis.

Claims 73-80 (canceled).